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Ana Luís Pimenta de Almeida Ferreira

Psoríase no idoso: estudo observacional do registo DERMA.PT

Psoriasis in the elderly: observational study from DERMA.PT registry

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NOME

Ana Luís Pimenta de Almeida Fenneina

NÚMERO DE ESTUDANTE	E-MAIL
201103634	alpimenta.fenneina@gmail.com

DESIGNAÇÃO DA ÁREA DO PROJECTO

Dermatologia e Venereologia

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Psoríase no idoso: estudo observacional do registo DERMA.PT

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Aos meus pais.

Às minhas irmãs.

Psoriasis in the elderly: observational study from DERMA.PT registry

Ferreira AL, Azevedo F MD[1], Magina S MD, PhD[1, 2]

Centro Hospitalar São João, EPE

[1] Serviço de Dermatologia e Venereologia, Centro Hospitalar São João, Porto, Portugal

[2] Departamento de Biomedicina, Faculdade de Medicina da Universidade do Porto, Porto, Portugal

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ABSTRACT

Background Elderly psoriasis (PsO) patients are a growing population, frequentely excluded from clinical trials and described as a high-risk group for adverse events. Our aim is to describe safety and clinical impact of systemic PsO therapy in elderly patients treated with methotrexate or biologic drugs.

Methods Elderly patients (≥65 years-old) receiving systemic PsO treatment at a reference centre, registered to DERMA.PT, were grouped according to current therapy – patients receiving methotrexate (MTX) and patients receiving biologic drugs (BIO). Patients' epidemiological and clinical characteristics were described. Adverse events of previous and current therapies were registered and compared according to treatment at that time. Comorbidities were analyzed within the elderly groups and compared to non-elderly patients also receiving systemic therapy.

Results 43 (20.0%) of 215 registered patients were elderly, 23 receiving methotrexate (MTX) and 20 receiving biologic drugs (BIO) with similar characteristics. BIO patients registered a significantly higher frequency of previous treatments than MTX patients (BIO 75.0% vs. MTX 8.7%, $P < 0.001$). Total number of adverse events in both groups was not different ($P < 0.101$). In general, elderly patients had higher frequency of comorbidities than non-elderly patients.

Conclusions Total number of adverse events was similar between MTX and BIO patients, the majority of which were non-serious and merely required dose adjustments. These results are reassuring, contributing to the demystification of the use of systemic treatments in the elderly and providing the best possible care to this growing group of patients.

INTRODUCTION

Psoriasis (PsO) is a chronic inflamatory skin disease that affects 2-3% of the global population. Besides the envolvement of the skin, patients may also have Psoriatic Arthritis (PsA) and high prevalence of cardiovascular comorbidities, such as dyslipidaemia and hypertension. Some studies have demonstrated that PsO is an independent risk factor for the development of diabetes and other components of metabolic syndrome, indirectly serving as a risk factor for cardiovascular disease. [1] The typical pattern of remission and recurrence of PsO depends on several precipitant factors such as emotional and physical stress, leading to low self-esteem, anxiety and depression.[2]

PsO can be diagnosed at any age, typically in a bimodal pattern: in young adults (15-25 years-old) and later, between 50 and 60 years-old.[3] The distinction between early-onset (<40 years-old) and late-onset (≥40 years-old) disease is also frequently mentioned due to differences in genetic components and clinical presentation[4], but without current recognised practical application on a daily basis.

Population ageing has been an increasing trend in Europe, particularly in Portugal, where 19% of the population was ≥65 years-old in 2011.[5] The present scenarios pose challenges for the therapeutic approach for chronic inflammatory diseases, such as PsO.

Nowadays, patients have been able to maintain a longstanding state of remission due to the introduction of classic or biotechnological systemic drugs. It is well-documented in several studies including non-elderly (<65 years-old) patients with PsO, PsA, Rheumatoid Arthritis (RA) and Ankylosing Spondylitis (AS).[6] However, the

elderly (≥ 65 years-old) are a subset of patients frequently excluded from clinical trials due to the higher number of comorbidities and polymedication, which pose them as a high-risk group for drug interactions and serious adverse events. Thus, there is lack of information about safety and effectiveness of avaliable treatments for PsO in the elderly, particularly about systemic drugs. Furthermore, some studies have demonstrated that dermatologists are still very reluctant to medicate these patients with systemic drugs, narrowing their treatment options to topical agents, in order to minimize possible adverse events, but compromising treatment effectiveness and only achieving a moderate control of the disease.[7]

Recently, progress has been made with several observational studies in older patients.[3,8-11] Nevertheless, clinical trials specifically testing systemic drugs in the elderly are scarse, creating an obstacle in reaching consensus regarding drug doses and possible therapeutic combinations, in order to improve life quality and control of the disease in this population.

Our aim is to describe safety and clinical impact of systemic PsO therapy, comparing elderly patients treated with methotrexate and elderly patients treated with biotechnological drugs.

MATERIAL AND METHODS

This retrospective observational study is designed to be based on the portuguese registry database for psoriatic diseases, DERMA.PT. Data collection from this platform assures a real-life scenario, data quality and fast data collection. The use of DERMA.PT information is authorised by the local ethics commitee, following International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, according to the Helsinki Declaration and ensuring maximum confidentiality. We collected data until the 15th of March 2017.

Since the portuguese age of retirement is 65 years-old, we defined elderly patients as individuals who are 65 years-old or over. We selected elderly patients with moderate to severe PsO, registered to DERMA.PT, receiving isolated biotechnological drugs (etanercept, adalimumab, ustekinumab, infliximab, secukinumab or golimumab) or methotrexate, at Centro Hospitalar São João (CHSJ), Porto, Portugal, in March 2017. Our aim is to compare two subgroups of elderly individuals: patients treated with methotrexate (MTX) and patients treated with any isolated biotechnological drug (BIO). We exported information from DERMA.PT concerning patient characteristics (gender, date of birth, date of diagnosis of PsO, weight, height, type of PsO and comorbidities), previous and current systemic treatments, registered reason of withdrawl and adverse events. All events were considered, including ones caused by previous systemic treatments that are now terminated, and classified as non-severe adverse events (NSAE), with minor implications for the patient, not requiring any specific treatment or merely dose adjustments, and severe adverse events (SAE), if they were tumours, life-threatening events or motivated

hospitalization and/or surgery. Current age, age of onset and length of disease were calculated, based on date of birth and date of diagnosis of PsO. Body mass index (BMI) was calculated using current weight and height of each individual. Patients were classified as obese, overweight and normal BMI according to World Health Organization (WHO) definition.[12] Our definition of major cardiovascular events (MACE) included episodes of acute myocardial infaction (AMI), stroke, transient ischemic attack (TIA), deep (DVT) vein thrombosis and pulmonary embolism (PE). Baseline and current disease activity were measured through the Psoriasis Area Severity Index (PASI), Body Surface Area (BSA) and Dermatology Quality of Life Index (DLQI).

Information from non-elderly patients (<65 years-old) regarding comorbidities was also collected, in order to ascertain differences between the two age groups.

5 non-elderly patients (2 females, 3 males) were excluded from this study because they had withdrawled systemic treatment during 2016. 3 elderly patients were excluded from statistical analysis because they are currently receiving treatment with methotrexate in association with a biologic drug.

Quantitative data are expressed as means and standard deviations (SD), while qualitative data are expressed as n (%). Means were compared using Student's t-test and frequencies with the $\chi 2$ test or Fisher's exact test when necessary. A $P < 0.05$ was considered as statistically significant. Statistical analyses were computed with IBM® SPSS® Statistics, Version 24.

RESULTS

CHSJ had two hundred twenty-three patients registered to DERMA.PT in March 2017, two hundred fifteen of which were eligible for our study. Eighty-two females (38.1%) and one hundred thirty-six males (63.2%), one hundred seventy-two non-elderly (80.0%) and forty-three elderly patients (20.0%).

Our study population included thirty males (79.8%) and thirteen females (30.2%), with mean age of 71.0 ± 4.7 years-old. Twenty-three patients were receiving systemic treatment with methotrexate (MTX group) and twenty with biologic drugs (BIO group). Within BIO patients, eight were receiving treatment with etanercept, eight with adalimumab, three with ustekinumab and one with secukinumab (Table 1).

Differences in mean age between MTX and BIO patients (70.6 ± 5.0 vs. 71.4 ± 4.5) were not statistically significant (P < 0.566), as well as age of onset (42.0 ± 19.5 vs. 39.7 ± 15.1, P < 0.672) and length of disease (28.2 ± 18.1 vs. 31.4 ± 14.6, P < 0.533) (Table 1). In both groups, the most frequent main clinical aspect of PsO was the presence of PsA (56.5% MTX vs. 75% BIO, P < 0.205). Body mass index (BMI) was not considered different between MTX and BIO patients (P < 0.775). 43.4% of MTX patients were obese and 60.0% of BIO patients were overweight. No differences were found between both groups regarding comorbidities. Hypertension (65.2%) and dyslipidaemia (65.2%) were the most common associated conditions in MTX patients and PsA (75.0%) and hypertension (65.0) were the most frequent comorbidities within BIO patients (Table 1). All comorbidities except ungueal dystrophy (22.7% vs. 11.6%), were more frequent in the elderly group, compared to

non-elderly individuals. On the one hand, cardiac valvular disease, Crohn's disease, hepatitis B and hepatitis C each had 1 case registered in the non-elderly group. On the other hand, ulcerative colitis had 1 case registered in the elderly group. (Table 2)

Considering previous therapies, the majority of patients in the BIO group had already been treated with other systemic drugs (MTX 8.7% vs. BIO 75.0%, $P < 0.001$). Fifteen BIO patients had tried at least one drug and two patients had experimented with 3 previous treatments. Twenty-one patients (91.3%) from the MTX group were naïve for previous systemic therapies (Table 1).

Both groups included patients with moderate to severe PsO with high baseline PASI, BSA and DLQI. However, there were statistically significant differences between both groups. BIO patients generally had higher baseline PASI (21.1 ± 13.0 vs. 12.3 ± 5.4, $P < 0.013$) and DLQI (15.8 ± 3.6 vs. 12.9 ± 3.3, $P < 0.025$), and lower current DLQI (0.8 ± 0.8 vs. 2.3 ± 2.6, $P < 0.026$) and BSA (1.0 ± 1.1 vs. 7.3 ± 9.5, $P < 0.008$). (Table 1)

A total of seventy-three adverse events were registered, thrity in the MTX group (23 NSAE and 7 SAE) and forty-three in the BIO group (34 NSAE and 9 SAE), without statistically significant differences between total events in both groups ($P < 0.101$). MTX patients registered a higher proportion of SAE than BIO patients. Both groups registered a minimum of zero events, with maximum of six events in MTX patients and seven events in BIO patients (Table 3). It should be noted the existence of 7 cases in MTX-treated patients and 3 cases in BIO-treated patients without any reports of adverse events. Distribution of adverse events according to active treatment at the moment of occurrence is presented in Table 4. For a total of

seventy-three reported adverse events, thirty-five (47.9%) occurred with methotrexate, seventeen (23.3%) with adalimumab, eleven (15.1%) with etanercept, six (8.2%) with ustekinumab and the remainder divided by infliximab (1.4%), methotrexate+adalimumab (1.4%) and methotrexate+infliximab (2.7%). The most frequent event was hepatotoxicity with twenty-five (34.2%) reports, followed by viral respiratory infections with twelve (16.4%) reports and bacterial respiratory infections with six (8.2%) reports.

At last, it is worth mentioning the three elderly patients, all male with ages comprised between 68 and 76 years-old, receiving treatment with an association of low doses of methotrexate and standard doses of biologic drugs, one of etanercept, one of adalimumab and one of infliximab. It is interesting to note that only one had a serious adverse event that conditioned hospitalization, in this case a fracture of the femur during treatment with etanercept in 2014. Overall, the three had a total of 5 adverse events, 4 of which were non-serious (1 episode of hepatotoxicity and 3 episodes of viral respiratory infection). All three have hypertension, PsA and are overweight.

COMMENT

Systemic treatments, particularly biologic drugs, have gradually become an important therapeutic option in the management of psoriatic patients. Safety and efficacy of systemic drugs are well-established in several studies performed with rheumatology patients.[6,13-18] However, information about psoriatic patients is still scarce[19-25] and elderly individuals continue to be frequently excluded from clinical trials, incurring the risk of being largely undertreated regarding their condition.

In the present study, our population from DERMA.PT is composed by two hundred fifteen patients, with 20% of elderly individuals. In spite of being a small size sample, the proportion of patients aged equal and over 65 years-old is double the ones described in other similar european studies, in France and Spain, where elderly patients represent 9.5% and 9.8%, respectively, of the population.[3,10] It is also worth mentioning that this proportion of older patients goes in line with the current portuguese population, which in 2011 had 19% of elderly individuals.[5] The distribution according to gender shows a higher number of male patients (63.2%), even within elderly patients (79.8%), which goes against some studies that describe a higher prevalence of elderly female patients.[3,10]

Regarding comorbidities, we observed that older patients tend to have more associated diseases than younger ones. The only exception is ungueal dystrophy, which in our population was more frequent in the non-elderly group. 20-30% of psoriatic patients tend to develop PsA after approximately 10 years of disease.[26] Both MTX and BIO groups had higher prevalences of PsA compared to younger

individuals, with a total of 28 (65.1%) elderly and 78 (45.3%) non-elderly patients affected by this comorbidity.

PsO is considered an independent risk factor for the development of several components of metabolic syndrome such as dyslipidaemia, hypertension, diabetes and obesity.[1] Phan et al. reported a higher prevalence of these conditions in association with greater age.[22] Age alone is a well-known contributor for numerous disorders, including cancer and cardiovascular disease. Accordingly, it was not surprising that these comorbidities had higher prevalence in the elderly group in the present study (Table 4).

The higher incidence of comorbidities in elderly patients is generally assumed as a risk factor for adverse events, but it is still unclear to what extent should we exclude these patients from systemic treatment because of their associated conditions. In our study, we found no differences between total number of adverse events in MTX and BIO patients ($P < 0.101$), despite the fact that comorbidities were, in general, more frequent in elderly patients. Furthermore, when analyzing the incidence of adverse events in older individuals, some studies state that elderly and non-elderly patients have similar rates of total reported adverse events, with a higher incidence of severe ones.[10,14] This could possibly become a turning point in management of moderate to severe PsO in older patients. However, across the globe, guidelines for clinical practice regarding systemic therapy for PsO are not uniform and depend on geographical location.[27] Consequentely, in light of limited reliable information, dermatologists continue to be reluctant to medicate elderly patients with systemic drugs, in fear of adverse events and drug interactions, leading to undertreatment

and moderate control of the disease.[7] Surely, adverse effects of treatment should always be considered when deciding whether to prescribe systemic drugs, notwithstanding each patient is unique and should be managed according to their illness and comorbidities in association with follow-up program with close monitoring of patients. In both MTX and BIO patients, the majority of adverse events were non-serious and were treated with small dose adjustments or short periods of discontinuation, in order to minimize the impact on PsO therapy. This information is reassuring and testifies to the ease of managing side effects if the patient monitoring program is effective.

In regard to past systemic therapies, BIO patients registered a significantly higher frequency of previous treatments than MTX patients (BIO 75.0% vs. MTX 8.7%, $P < 0.001$). However, this is in agreement with the therapeutic escalation performed in our institution.

Systemic therapy is recommended in cases of moderate to severe PsO, with PASI, BSA and DLQI scores reflecting an active disease, with a negative impact on the patient's psychological state and ability to perform activities of daily living.[2,28,29] It is important to emphasize that elderly patients may have as serious a disease as non-elderly people, benefiting greatly from systemic treatment, with higher number of longstanding remissions and longer periods between relapses, as already well-established for other age groups and other chronic diseases, such as RA[7,8,10,11,18,24], and our results turned out to reflect these aspects (Table 1).

This study might have some characteristic limitations of retrospective studies, such as: selection bias (both patient and treatment selection bias), information

bias, confounding (absence of data on potential confounding factors if the data was not recorded in the past), ascertainment/enrollment bias, lost to follow-up and censored observations.

Considering the aging of the population in developed countries, it becomes even more important to evaluate the suffering of the elderly with certain chronic illnesses like PsO. As in other diseases such as hypertension and diabetes, in which therapies are already targeted for a specific age group and its comorbidities, it is necessary to optimize the treatment of the elderly also in PsO, taking into account the whole set of associated diseases. Our results are reassuring considering that older patients tend to have more comorbidities and effectively are at greater risk of drug interactions due to polimedication. Along with other similar conclusions from recent studies[3,7,10], this could become a turning point in management of moderate to severe PsO in the elderly, contributing to the demystification of the use of systemic treatments in these conditions and providing the best possble care and quality of life to this growing group of patients.

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Table 1 – Epidemiological, clinical characteristics, treatments and comorbidities of elderly psoriatic patients – MTX group vs. BIO group

	MTX	**BIO**	**P-value**
	n=23	n=20	
Length of treatment (months), mean ± SD	52.6 ± 34.1	59.3 ± 37.6	
Age (years), mean ± SD	70.6 ± 5.0	71.4 ± 4.5	0.566
Gender, n (%)			0.975
Male	16 (69.6)	14 (70.0)	
Age of onset (year), mean ± SD	42.0 ± 19.5	39.7 ± 15.1	0.672
Length of disease (year), mean ± SD	28.2 ± 18.1	31.4 ± 14.6	0.533
Main clinical aspect of PsO, n (%)			0.205
Plaque PsO	10 (43.5)	5 (25.0)	
PsA, n (%)	13 (56.5)	15 (75.0)	
BMI, n (%)			0.775
Normal (18.50 ≤ BMI < 25 kg/m^2)	4 (17.3)	2 (10.0)	
Overweight (≥ 25 kg/m^2)	9 (39.1)	12 (60.0)	
Obesity (≥ 30 kg/m^2)	10 (43.4)	6 (30.0)	
Disease activity, mean ± SD			
Baseline PASI	12.3 ± 5.4	21.1 ± 13.0	**0.013****
Current PASI	3.8 ± 3.6	2.0 ± 2.4	0.078
Baseline DLQI	12.9 ± 3.3	15.8 ± 3.6	**0.025****
Current DLQI	2.3 ± 2.6	0.8 ± 0.8	**0.026****
Baseline BSA	20.4 ± 10.6	40.4 ± 32.5	0.051
Current BSA	7.3 ± 9.5	1.0 ± 1.1	**0.008****
Previous systemic treatment, n (%)			**<0.005***
Yes	2 (8.7)	15 (75.0)	
No	21 (91.3)	5 (25.0)	
Number of previous treatments, n (%)			**<0.005*****
0	21 (91.3)	5 (30.4)	
1	2 (8.7)	10 (47.8)	
2	0 (0.0)	3 (13.0)	
3	0 (0.0)	2 (8.7)	
Current treatment, n (%)			
Methotrexate	23 (100)	0 (0.0)	

Etanercept	0 (0.0)	8 (40.0)
Adalimumab	0 (0.0)	8 (40.0)
Infliximab	0 (0.0)	0 (0.0)
Ustekinumab	0 (0.0)	3 (15.0)
Secukinumab	0 (0.0)	1 (5.0)
Golimumab	0 (0.0)	0 (0.0)
Comorbidities, n (%)		
PsA	13 (56.5)	15 (75.0)
Diabetes	5 (21.7)	4 (20.0)
Hypertension	15 (65.2)	13 (65.0)
Dyslipidaemia	15 (65.2)	10 (50.0)
Obesity	10 (43.4)	6 (30.0)
MACE	2 (8.7)	1 (5.0)
Skin cancer	2 (8.7)	3 (15.0)
Non-skin cancer	1 (4.3)	1 (5.0)

*Chi-Square Test, **ANOVA, ***Mann-Whitney U test

PsA, Psoriatic Arthritis; MACE, Major Cardiovascular Events; PASI, Psoriasis Area Severity Index; BSA, Body Surface Area; DLQI, Dermatology Quality of Life Index

Table 2 – Comorbidities in elderly and non-elderly patients, n (%)

	Non-Elderly (<65 yo)	**Elderly (≥65 yo)**
	n=172	n=43
PsA	78 (45.3)	28 (65.1)
Obesity	32 (18.6)	16 (37.2)
Hypertension	45 (26.2)	28 (65.1)
Diabetes	13 (7.6)	9 (20.9)
Dyslipidaemia	50 (29.1)	25 (58.1)
Ischaemic cardiomyopathy	1 (0.6)	5 (11.6)
Chronic heart failure	0 (0.0)	2 (4.6)
Atrial Fibrillation	1 (0.6)	2 (4.6)
Valvular heart disease	1 (0.6)	0 (0.0)
Ulcerative colitis	0 (0.0)	1 (2.3)
Crohn's disease	1 (0.6)	0 (0.0)
Chronic hepatopathy	17 (9.9)	5 (11.6)
Hepatitis B	1 (0.6)	0 (0.0)
Hepatitis C	1 (0.6)	0 (0.0)
Dactylitis	8 (4.6)	4 (9.3)
Ungueal dystrophy	39 (22.7)	5 (11.6)
Skin cancer	1 (0.6)	5 (11.6)
Non-skin cancer	1 (0.6)	2 (4.6)
MACE	0 (0.0)	3 (7.0)
Chronic pulmonary disease	10 (5.8)	7 (16.3)
Renal disease	5 (2.9)	7 (16.3)
Depression/Anxiety	7 (4.1)	2 (4.6)
Hypothyroidism	0 (0.0)	2 (4.6)
Hyperuricemia	3 (1.7)	4 (9.3)
Other skin disorders	4 (2.3)	4 (9.3)

PsA, Psoriatic Arthritis; MACE, Major Cardiovascular Events

Table 3 – Frequency and severity of adverse events in MTX and BIO patients

	MTX	**BIO**	**P-value**
	n= 23	n=20	
Total events, n (%)	30 (100)	43 (100)	
Number of events, mean ± SD	1.3 ± 1.5	2.2 ± 1.8	0.101
Minimum	0	0	
Maximum	6	7	
Severity, n (%)			
NSAE	23 (76.7)	34 (79.1)	
SAE	7 (23.3)	9 (20.9)	

NSAE, Non-severe adverse events; SAE, Severe adverse events

Table 4 – Number of adverse events according to active systemic treatment at the time of occurrence, n (%) per total number of events.

	Mtx	Eta	Ada	Inf	Ustek	Mtx+ Ada	Mtx+ Inf	Total
Hepatotoxicity	19 (26.0)	2 (2.7)	2 (2.7)	0 (0.0)	2 (2.7)	0 (0.0)	0 (0.0)	25 (34.2)
Skin Infection								
Bacterial	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Fungal	3 (4.1)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (5.5)
Viral	1 (1.4)	1 (1.4)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.1)
Respiratory infection								
Bacterial	1 (1.4)	1 (1.4)	2 (2.7)	0 (0.0)	1 (1.4)	1 (1.4)	0 (0.0)	6 (8.2)
Viral	0 (0.0)	5 (6.8)	4 (5.5)	0 (0.0)	2 (2.7)	0 (0.0)	1 (1.4)	12 (16.4)
GI infection								
Fungal	1 (1.4)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.7)
Acute biliary pancreatitis	1 (1.4)	1 (1.4)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.1)
Skin cancer	0 (0.0)	1 (1.4)	1 (1.4)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	3 (4.1)
Non-skin cancer	0 (0.0)	0 (0.0)	1 (1.4)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.7)
MACE	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Bone fracture	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Hemoperitoneum	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Appendicitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)	1 (1.4)
GI intolerance	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Head injury	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Cytopenia	2 (2.7)	0 (0.0)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (4.1)
Pulmonary toxicity	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Pyelonephritis	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Acute HF	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.4)
Total	35 (47.9)	11 (15.1)	17 (23.3)	1 (1.4)	6 (8.2)	1 (1.4)	2 (2.7)	73 (100)

Mtx, Methotrexate; Eta, Etanercept; Ada, Adalimumab; Ustek, Ustekinumab; Inf, Infliximab

HF, Heart Failure; GI, Gastrointestinal; MACE, Major Cardiovascular Events

AGRADECIMENTOS

Gostaria de agradecer à minha orientadora, a Professora Dr.ª Sofia Magina, pela disponibilidade e revisão crítica que permitiram o desenvolvimento deste projeto.

ANEXOS

1. Autorização CES – Registo Nacional de Doentes com Psoríase - DERMA.PT

2. Normas de publicação International Journal of Dermatology

Parecer da Comissão de Ética para a Saúde do

Centro Hospitalar de São João / Faculdade de Medicina da Universidade do Porto

Título do Projecto: Registo Nacional de Doentes com Psoríase – Derma.pt

Nome da Investigadora Principal: Prof.ª Doutora Sofia Magina

Serviço onde decorre o Estudo: Dermatologia. Tem a autorização da Dra. Filomena Azevedo.

Objectivo do Estudo:

Criar uma plataforma nacional de registo de dados de doentes com psoríase. Promovida pela Sociedade Portuguesa de Dermatologia e Venereologia.

Concepção e Pertinência do estudo:

Serão incluídos no estudo todos os doentes diagnosticados com psoríase candidatos à prescrição de produtos biológicos ou que já se encontrem em tratamento. Consta da informação recolhida pelo médico assistente dados sociodemográficos (idade, mês e ano de nascimento, sexo, raça, nacionalidade e naturalidade, escolaridade, profissão, situação laboral antes do início da doença e actualmente), dados antropométricos (peso, altura, IMC), sinais vitais, dados sobre a psoríase, lesões cutâneas, tabagismo, consumo de álcool, resultados de análises laboratoriais, imagiologia, medicação e terapêutica biológica.

Benefício/risco:

A recolha de informação permitirá criar uma base de dados nacional, que reunirá a informação relativa a cada doente de um modo holístico e global, evitando falhas por lapso de omissão de informação. Não existem riscos ou incómodos para os doentes.

Confidencialidade dos dados:

Os dados serão recolhidos num caderno de recolha de dados em formato electrónico e inseridos centralmente num servidor externo da WebSP – Comércio e Prestação de Serviços Informáticos, Lda., localizado em Portugal. O médico assistente, investigador no estudo, solicitará consentimento informado, cuja declaração será conservada no processo clínico do utente. No 'caderno de recolha de dados' não há identificação nominal do titular, sendo esta codificada. A chave desta codificação só é conhecida pelo médico assistente, ou pelo coordenador do Centro.

Respeito pela liberdade e autonomia do sujeito de ensaio:

A liberdade em participar está salvaguardada, e a informação é adequada.

***Curriculum* da investigadora**: Adequado à investigação.

Data previsível da conclusão do estudo: Sem data previsível de conclusão.

Conclusão: Proponho um parecer favorável à realização deste projecto de investigação.

Porto, 27 de Abril de 2015

O Relator

Doutor Pedro Brito

Direcção Clínica
11 / 5 / 2015

CES 130-15

AUTORIZADO

CONSELHO DE ADMINISTRAÇÃO EM REUNIÃO DE 13 MAI 2015
Presidente do Conselho de Administração
(Prof. Doutor António Ferreira)
Directora Clínica | Enfermeira Directora | Vogal Executivo | Vogal Executivo
(Dr. Marcelo Sousa) | (Enfermeira Beatrice Portela) | (Dr. João Oliveira) | (Dr. Arnaldo Ferreira)

Exmo. Senhor
Presidente do Conselho de Administração do
Centro Hospitalar de S. João – EPE

Assunto: Pedido de autorização para realização de estudo/projecto de investigação

Nome do Investigador Principal: Prof. Sofia Magina

Título do projecto de investigação: Registo Nacional de Doentes com Psoríase – Derma.pt

Pretendendo realizar no(s) Serviço(s) de DERMATOLOGIA do Centro Hospitalar de S. João – EPE o estudo/projecto de investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efectivação.

Para o efeito, anexa toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar de S. João respeitante a estudos/projectos de investigação, à qual endereçou pedido de apreciação e parecer.

Com os melhores cumprimentos.

Porto, 12 / Abril / 2015

Hospitalar São João
FMG de Medicina
Dermatologia e Venereologia
Dra. Sofia Magina
[illegible]25768

O INVESTIGADOR/PROMOTOR

7. SEGURO

a. *Este estudo/projecto de investigação prevê intervenção clínica que implique a existência de um seguro para os participantes?*

SIM ☐ (Se sim, junte, por favor, cópia da Apólice de Seguro respectiva)

NÃO ☐

NÃO APLICÁVEL ☒

8. TERMO DE RESPONSABILIDADE

Eu, Sofia Magina,

abaixo-assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (com as emendas de Tóquio 1975, Veneza 1983, Hong-Kong 1989, Somerset West 1996 e Edimburgo 2000) e da Organização Mundial da Saúde, no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo no decurso do actual internamento ou da mesma consulta.

Porto, 13 / Abril / 2015

Centro Hospitalar São João
UAG de Medicina
Dermatologia e Venereologia
Dra. Sofia Magina

O Investigador Principal

PARECER DA COMISSÃO DE ÉTICA PARA A SAÚDE DO CENTRO HOSPITALAR DE S. JOÃO/FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO

emitido na reunião plenária da CES 24 de Abril de 2015

A Comissão de Ética para a Saúde APROVA por unanimidade o parecer do Relator, pelo que nada tem a opor à realização deste projecto de investigação.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

NORMAS DE PUBLICAÇÃO INTERNATIONAL JOURNAL OF DERMATOLOGY

Author Guidelines

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Published monthly, the *International Journal of Dermatology* (*IJD*) is specifically designed to provide dermatologists around the world with a regular, up-to-date source of information on all aspects of the diagnosis and management of skin diseases. Accepted articles regularly cover clinical trials, education, morphology, pharmacology and therapeutics, case reports, and reviews. Additional features include tropical medicine reports, news, correspondence, and proceedings and transactions.

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On a Human Scale* (by invitation only)
An article that relates to social, economic, cultural, artistic and humanitarian aspects of medicine. The length of the article should not exceed 1200 words including a short summary of the topic addressed. A brief author biography and photo should be submitted with the article. If you have a topic that you feel would fit nicely in this section, please send a note to ijdermatol@mayo.edu for approval to submit.

Pharmacology and Therapeutics
An article relating to the treatment of diseases and to the pharmacology of dermatologically-related drugs. (Can include Clinical Trials, Reviews, Reports, Case Reports and Correspondence. The latter is preferred for reports of adverse drug reactions.) When referring to a drug, please use the generic name approved by the United States Food and Drug Administration or recognized as the United States Adopted Name. At the end of the manuscript, please list the American Trade names.

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An article on the history of dermatology or skin diseases; also a biographic account of an historic or noteworthy figure in dermatology.

Report
An original article including, whenever possible, an Introduction, Materials and Methods or Case Report(s), Results, Comment, and References. A Structured Abstract of not more than 250 words must be included and should consist of four paragraphs labeled Background, Methods, Results, and Conclusions. Also, it should describe the problem studied, how the study was performed, the main results, and what the author(s) concluded from the results. The article should range from 2500-3000 words.

Review
A major didactic article that clarifies and summarizes the existing knowledge in a particular field. It should not be an exhaustive review of the literature, and references should not exceed 50 in number. Tables, diagrams, and selected figures are often helpful and prefered. The length is left to the judgment of the author, although it generally should not exceed 5000 words. Topics may include updates in clinically relevant basic science and cutaneous biology. A list of 10 questions should be listed at the end of the article to provide additional educational challenge to the reader. An abstract is required, though it need not be structured.

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An article dealing with the diseases and special problems encountered by dermatologists working in the tropics. Article submissions should follow the Report or Case Report format.

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By invitation only. This contribution to the journal should be 700–1200 words in length with sufficient references to document important points. It is not essential that the contribution be heavily referenced as it is meant to serve as an update for dermatologists in various fields of medicine and is not portrayed to be an extensive or exhaustive review of the literature. However, it would be very helpful if pertinent and salient references are included, not only for documentation purposes, but also for additional reading.

Medical Genetics
Report, Review or Case Report format should be followed.

*No abstract required

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Submissions should be made online at the *IJD* ScholarOne Manuscripts site (formerly known as Manuscript Central). New users should first create an account (do not upload document files at this time). Once a user is logged onto the site, submissions should be made via the Author Center.

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Submission of a manuscript will be held to imply that it contains original unpublished work and is not being submitted for publication elsewhere at the same time. The author must supply a full statement to the Editor about all submissions and previous reports that might be regarded as redundant or duplicate publication of the same or very similar work.

4. PREPARATION OF MANUSCRIPTS

Manuscripts must be written in English and must comply with these instructions in every detail.

Text should be supplied in a word processed format such as Microsoft Word for Windows. Charts and tables are considered textual and should be supplied in the same format. Figures (illustrations, diagrams, photographs) should be supplied in gif, jpeg, tif or eps format.

All manuscripts must be typed in 12 pt font with lines double spaced and margins of at least 2.5 cm.

Abbreviations must be defined when first used, both in the abstract and in the main text.

Manuscripts must be as succinct as possible. Text must comply with the word and figure limits defined in Section 2. If authors consider that a manuscript should not conform to the limits specified, exceptionally good reasons must be clearly provided in a cover letter accompanying the submission. Repetition of information or data in different sections of the manuscript must be carefully avoided.

Manuscripts should, where appropriate, include:

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The first page of all manuscripts should contain the following information:
1) the title of the paper
2) surnames (family names),initials of each author, and their degree (if any)
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5) manuscript word count (excluding abstract and references), table and figure count
7) any conflict of interest disclosures (see Section 5)
8) a running head not exceeding 50 characters

Abstracts
Authors submitting Reports should note that structured abstracts (maximum 250 words) are required. The structured abstract should adopt the format: Background, Methods, Results, Conclusions.

Review articles require abstracts (maximum 250 words) but they need not be structured.

Abstracts should not contain citations.

Text
This should in general, but not necessarily, be divided into sections with the headings: Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References, Tables, Table and figure legends. Figures should be submitted as separate files. The acknowledgements should include a statement of all funding sources that supported the work.

Please submit the full text of the manuscript, including the abstract, references, tables and legends as a single document. The title page may be included as page 1 of the main manuscript document or can be uploaded as a separate file, but must be included.

Tables and Figures
Tables should not be inserted in the appropriate place in the text but should be included at the end of the manuscript, each on a separate page.

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Tables and figures should be referred to in text as follows: Fig. 1, Figs. 2–4; Table 1, Tables 2 and 3. The place at which a table or figure is to be inserted in the printed text should be indicated clearly on a manuscript. Each table and/or figure must have a legend that explains its purpose without reference to the text. Where a figure has more than one panel, each panel should be labelled in the top left-hand corner using lower case letters in parentheses i.e. '(a)', '(b)' etc., and a brief description of each panel given in the figure legend. When using histology figures, the stain type and magnification level must be included in the legend.

Only figures of excellent quality will be considered for publication. The Journal will publish color photographs free of charge subject to editorial approval. When an individual is

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Format references as below, using standard (Medline) abbreviations for journal titles. When there are more than four authors, include the first three authors followed by *et al*.

1. de Berker DAR, Baran R, Dawber RPR. The Nail in Dermatological Diseases. In: *Baran and Dawber's Diseases of the Nails and their Management* (Baran R, Dawber RPR, de Berker DAR, Haneke E, Tosti, A, eds), 3rd edn. Oxford: Blackwell Science Ltd., 2001: 172–92.
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4. Smith A. (1999) Select committee report into social care in the community [WWW document]. URL http://www.dhss.gov.uk/reports/report015285.html [accessed on 7 November 2003].

5. DECLARATIONS

Original Publication
Submission of a manuscript will be held to imply that it contains original unpublished work and is not being submitted for publication elsewhere at the same time. The author must supply a full statement to the Editor about all submissions and previous reports that might be regarded as redundant or duplicate publication of the same or very similar work.

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When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983. Do not use patients' names, initials or hospital numbers, especially in illustrative material. When reporting experiments on animals, indicate whether the institution's or a national research council's guide for, or any national law on, the care and use of laboratory animals was followed. A statement describing explicitly the ethical background to the studies being reported should be included in all manuscripts in the Materials and Methods section. Ethics committee or institutional review board approval should be stated.

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Professor Rokea A. el-Azhary
Editor-in-Chief
Mayo Clinic E-5A
200 First Street SW
Rochester MN 55905
USA
Tel: +1 507 538-8249
Fax: +1 507 284 2072
E-mail: IntJDerm@gmail.com